

<b>PTO/SB/08A</b> <b>INFORMATION DISCLOSURE</b> <b>STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		<b>Complete if Known</b>	
		Application Number	10/007,450
		Filing Date	November 5, 2001
		Confirmation Number	3348
		First Named Inventor	Douglas F. Covey
		Group Art Unit	1616
		Examiner Name	Sabiha Naim Qazi
Sheet	1	of	1
		Attorney Docket No.	WSHU 2036.1

## U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code <sup>2</sup> (if known)		
<i>SLB</i>	57	5,552,395		Gemmill, Jr. et al.	09-03-1996

## FOREIGN PATENT DOCUMENTS

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Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	T <sup>6</sup>
		Office	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)			
	58	DE	199 17 930	A1	Schering AG	10-19-2000	

## OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
<i>SC/BS</i>	59	P.S. GREEN et al. "ENT-Estradiol Exerts Neuroprotective Effects in vitro and in vivo" Society for Neuroscience Abstracts, Vol. 25, No. 1/2 (10/23/99) p. 1849.	
<i>SC/BS</i>	60	C. BEHL et al. "Neuroprotection against oxidative stress by estrogens: structure-activity relationship" Molecular Pharmacology, Vol. 51, No. 4 (1997) pp. 535-541.	
<i>SC/BS</i>	61	Partial International Search Report from Application No. PCT/US01/47202 dated March 7, 2003.	

Examiner Signature	SABINA Q.M.ZI	Date Considered	6/28/03
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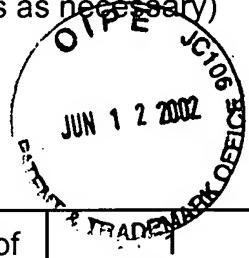
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		Examiner Name	Barbara P. Radio <i>QA2-1</i>
Sheet	1	of	Attorney Docket No.
		TRADEMARK OFFICE	WSHU 2036.1

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Sheet 1 of 5

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Confirmation Number	3348 <i>H.S.</i>
First Named Inventor	Douglas F. Covey
Group Art Unit	1616
Examiner Name	<u>Barbara P. Badio</u> <i>Q82</i>
Attorney Docket No.	WSHU 2036.1

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	1	3,472,885		Bucourt et al.	10-14-1969
	2	4,330,540		Zeelen	05-18-1982
	3	4,617,298		Bodor et al.	10-14-1986
	4	4,786,647		Simpkins et al.	11-22-1988
	5	5,554,601		Simpkins et al.	09-10-1996
	6	5,554,604		Bonfils et al.	10-10-1996
	7	5,679,668		Bonfils et al.	10-21-1997
	8	5,824,672		Simpkins et al.	10-20-1998
	9	5,843,934		Simpkins	12-01-1998
<i>SL</i>	10	5,859,001		Simpkins et al.	01-12-1999
	11	5,877,169		Simpkins	03-02-1999
	12	5,914,325		Droescher et al.	06-22-1999
	13	5,939,407		Landfield	08-17-1999
	14	5,972,923		Simpkins et al.	10-26-1999

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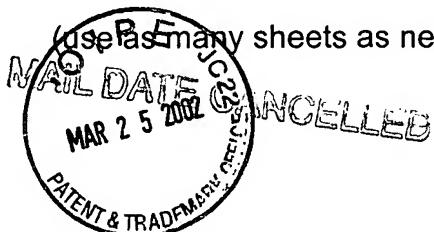
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Group Art Unit	1616
Examiner Name	Barbara P. Radio QAZ/5

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15	6,197,833	B1	Simpkins et al.	03-06-2001
16	6,207,658	B1	Simpkins et al.	03-27-2001
17	6,265,147	B1	Mobley et al.	07-24-2001

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		Office	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)			
	18	CA	1 167 837		Akzo N.V.	05-22-1984	
	19	EP	0 069 424	B1	Akzo N.V.	01-12-1983	
	20	GB	1 298 587		American Home Products Corporation	12-06-1972	
	21	WO	95/13076	A1	JENAPHARM GMBH	05-18-1995	
	22	WO	97/03661	A1	University of Florida Research Foundation, Incorporated	02-06-1997	
SB	23	WO	99/26630	A1	University of Florida Research Foundation, Incorporated	06-03-1999	
	24	WO	00/63228	A1	Schering Aktiengesellschaft	10-26-2000	
	25	WO	01/10430	A2	University of Florida Research Foundation, Inc.	02-15-2001	

Examiner Signature	Sebile Qaz	Date Considered	9/8/03
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Sheet 3 of 5

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First Named Inventor	Douglas F. Covey
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Examiner Name	Barbara P. Badio
Attorney Docket No.	WSHU 2036.1

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## OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
	26	Akhter et al., Safety Study of Tirlazad Mesylate in Patients With Acute Ischemic Stroke (STIPAS) Stroke, Vol. 25, No. 2 (1994) p. 418-423.	
	27	A. ALLAIS et al. "3-( $\beta$ -Dialkylaminoethoxy)estra-1,3,5(10)-trienes" Chemical Abstracts, Vol. 70, No. 25; Abstract No. 115418e (1969) p. 381.	
	28	K. BARNIKOL-OETTLER et al. "Preparation of Estradiol 3-methyl Ether" Chemical Abstracts, Vol. 160, No. 25, Abstract No. 106:214199c (1987).	
	29	C. BEHL et al. "17- $\beta$ Estradiol Protects Neurons from Oxidative Stress-Induced Cell Death in vitro" Biochemical and Biophysical Research Communications, Vol. 216, No. 2 (1995) pp. 473-482.	
SOZ	30	G.C. BUZBY et al. "Totally Synthetic Steroid Hormones. XIII. The Chemical Resolution of Some Racemic Estrane, 13 $\beta$ -Ethylgonane, and 13 $\beta$ -n-Propylgonane Derivatives and the Preparation of Some Estrane and 13 $\beta$ -Ethylgonane Derivatives of Unnatural Configuration" Journal of Medicinal Chemistry, Vol. 10 (1967) pp. 199-204.	
	31	T. FAN et al. "ZYC-13, the enantiomer of 1,3,5(10)-estratriene 3-OL, exerts neuroprotective effects in vitro and in vivo" Presented at the 26th Soc. for Neuroscience Meeting, 11/4/00 to 11/9/00.	
	32	Y. GOODMAN et al. "Estrogens Attenuate and Corticosterone Exacerbates Excitotoxicity, Oxidative Injury, and Amyloid $\beta$ -Peptide Toxicity in Hippocampal Neurons" Journal of Neurochemistry, Vol. 66, No. 5 (1996) pp. 1836-1844.	
	33	P. GREEN et al. " The Nonfeminizing Enantiomer of 17 $\beta$ -Estradiol Exerts Protective Effects in Neuronal Cultures and a Rat Model of Cerebral Ischemia" Endocrinology, Vol. 142, No. 1 (2001) pp. 400-406.	
	34	HALL et al. "Sex Differences in Postischemic Neuronal Necrosis in Gerbils" J. Cer. Blood Flow Metab., Vol. 11 (1991) p. 292-298.	

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Sheet	4	of	Attorney Docket No.	WSHU 2036.1
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	35	H. KANEKO et al. "The Synthesis of 2- and 4-Alkoxymethylestrogenes" Chem. Pharm. Bull., Vol. 12, No. 2 (1964) pp. 196-203.
	36	M. A. LEVITT et al. "Reduction of Infarct Size During Myocardial Ischemia and Reperfusion by Lazaroid U-74500A, a Nonglucocorticoid 21-Aminosteroid" J. of Cardiovascular Pharmacology, Vol. 23, No. 1 (1994) pp. 136-140.
	37	W. LUNN et al. "The Adamantyl Carbonium Ion as a Dehydrogenating Agent, its Reactions with Estrone" Tetrahedron Letters, Vol. 24, No. 23 (1968) pp. 6773-6776.
<i>SO</i>	38	C. MILLER et al. "In vitro antioxidant effects of estrogens with a hindered 3-OH function on the copper-induced oxidation of low density lipoprotein" Steroids, Vol. 61 (1996) pp. 305-308.
	39	MOORADIAN "Antioxidant Properties of Steroids" J. Steroid Biochem. Molec. Biol., Vol. 45, No. 6 (1993) pp. 509-511.
	40	M. NAKANO et al. "Novel and Potent Biological Antioxidants on Membrane Phospholipid Peroxidation: 2-Hydroxy Estrone and 2-Hydroxy Estradiol" Biochemical and Biophysical Research Communications, Vol. 142, No. 3 (1987) pp. 919-924.
	41	E. NIKI et al. "Antioxidants in Relation to Lipid Peroxidation" Chemistry and Physics of Lipids, Vol. 44, Nos. 2-4 (1987) pp. 227-253.
	42	T. PATTON et al. "Estrogens. IV. The Synthesis of 2- and 4-Alkylestrones" Journal of Organic Chemistry, Vol. 27, No. 3 (1962) pp. 910-914.
	43	E. J. PEREZ et al. "762.7 - Structure-Activity Relationship of Estratrienes Against Glutamate Toxicity in a Mouse Hippocampal Cell Line" Presented at the 26th Soc. for Neuroscience Meeting, 11/4/00 to 11/9/00.
	44	L. PROKAI et al. "Synthesis and Biological Evaluation of 17 $\beta$ -Alkoxyestra-1,3,5(10)-trienes as Potential Neuroprotectants Against Oxidative Stress" J. Med. Chem., Vol. 44, No. 1 (2001) pp. 110-114.
	45	W. ROMER et al. "Novel estrogens and their radical scavenging effects, iron-chelating, and total antioxidative actives: 17 $\alpha$ -substituted analogs of $\Delta^{9(11)}$ -dehydro-17 $\beta$ -estradiol" Steroids, Vol. 62 (1997) pp. 688-694.

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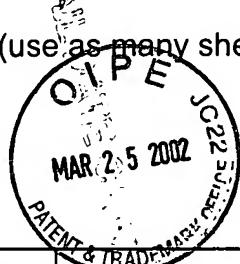
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46	W. ROMER et al. "Novel "scavestrogens" and their radical scavenging effects, iron-chelating, and total antioxidative actives: $\Delta^{8,9}$ -dehydro derivatives of 17- $\alpha$ -estradiol and 17 $\beta$ -estradiol" Steroids, Vol. 62 (1997) pp. 304-310.
47	A.G. SCHERING, "Preparation of ent-steroids as Selectively Effective Estrogens" Chemical Abstracts, Vol. 133, No. 21, Abstract No. 133:296594x (2000) p. 766-767.
48	A. SEELIG et al. "A method to determine the ability of drugs to diffuse through the blood-brain barrier" Proc. Natl. Acad. Sci. USA, Vol. 91 (1994) pp. 68-72.
49	L. TIETZE et al. "Synthesis of new 16-spirosteroids" Steroids, Vol. 59 (1994) pp. 305-309.
50	J. WILSON et al. "U83836E Reduces Secondary Brain Injury in a Rabbit Model of Cryogenic Trauma" Journal of Trauma, Vol. 39, No. 3 (1995) pp. 473-479.
51	A. WUNDERLI et al. "Geometry of the Activated Complex of the Thermal and Charge-Induced Aromatic Para to Ortho Claisen Rearrangement" Helvetica Chimica Acta, Vol. 56 (1973) pp. 989-1011.
52	S. XIA et al. "A Novel Estrogen Analog, Inactive at the Estrogen Receptor, is Neuroprotective" Presented at the 26th Soc. for Neuroscience Meeting, 11/4/00 to 11/9/00.
53	S-H. YANG et al. "Neuroprotective Effects of a Novel Non-Receptor Binding Estrogen Analogue During Stroke" Presented at the 26th Soc. for Neuroscience Meeting, 11/4/00 to 11/9/00.

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